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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/849,229

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EXAMINER

WARE, DEBORAH K

ART UNIT

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/849,229	<b>Applicant(s)</b> MAHADEVAN ET AL.	
	<b>Examiner</b> DEBBIE K. WARE	<b>Art Unit</b> 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 18 April 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 20-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 20-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Claims 20-24 are presented for reconsideration on the merits.

#### ***Response to Amendment***

The amendment filed March 24, 2008 and extension of time, and arguments therewith have been received and entered. Also the supplemental amendment filed April 18, 2008, has been received and entered. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balaraman et al (US 5,434,059), recited on enclosed PTO-1449 Form in view of Mizutani (US 4,009,264) and Hanson et al (5,700,669), both recited on enclosed PTO-892 Form.

Claims are drawn to a process for preparation of thrombolytic enzyme, Thrombinase.

Balaraman et al teach a process for preparation of thrombolytic enzyme, Thrombinase, see abstract. The process comprising culturing *Bacillus sphaericus* serotype H5a5b, see abstract, on a well known culture medium. Further, comprising removing cells, see column 2, line 55, performance of two step ultra filtration, see column 2, line 59, using molecular weight cut off membrane filters of 10,000 molecular weight (mw) and 30,000 mw, see column 5, lines 6 and 8. Also salting out with ammonium sulphate, note column 2, line 63, is performed. Further, dialysis and reconstituting buffer and dialysis steps are carried out as well, note column 3, lines 5-10 and lines 61-65. Decolorizing is also performed, note column 3, line 59. In addition, purifying is performed by ion exchange chromatography by gel filtration, note column 3, line 16. Thrombinase is, therefore, obtained note column 4, lines 23-35.

The claims differ from Balaraman et al in that the culture medium and the step of re-precipitating the precipitate using ice-cold acetone and thrombinase having a molecular weight range of 31,000-32,000 are not disclosed.

Mizutani teaches reaction product can be collected by precipitation with acetone and further, by repeating a cycle of dissolving precipitate in water for example, and

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reprecipitating it from acetone, the precipitate can be purified. Note column 9, lines 60-67.

Hanson et al teach a culture medium for microorganisms, and further, *Bacillus sphaericus* is disclosed, note column 6, line 54. *Bacillus* species are cultivated in medium comprising beef extract, peptones, sodium chloride, note column 7, lines 36-45. Furthermore, other ingredients for culture medium are disclosed which include sodium acetate, yeast extract, ammonium sulfate, etc., note column 9, lines 10-40.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the process steps of Balaraman et al using the reprecipitating step in ice-cold acetone and culture medium of Mizutani and Hanson et al, respectively because acetone is known to be used for purifying enzymes and the culture medium is well known to be useful for *Bacillus* species. The art clearly recognizes the usefulness of the reprecipitating step in acetone for purifying an enzyme as taught by Mizutani and for culturing *Bacillus* species in a culture medium as taught by Hanson et al.

Balaraman et al clearly teach culturing the *Bacillus sphaericus* serotype H5a5b in a well known culture medium of which Hanson et al clearly do teach and demonstrate to be well known. Hanson et al describe a culture medium which contains all of the same ingredients as claimed. To select soya peptone is clearly within the skill of an artisan. To obtain a Thrombinase between the range of 31,000 to 32,000 molecular weight is also well within the purview of an ordinary artisan. Therefore, although Balaraman et al

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identify a thrombinase of 18,500 molecular weight one of skill would have been motivated to obtain other thrombinase enzymes to enhance results of their process.

The pH is clearly recognized by the cited prior art and to vary the range of ammonium sulphate is a matter of selective optimization of the cited prior art and well within the skill of an ordinary artisan. Further, to provide for a selected ratio of acetone and crude enzyme is also within the skill of an ordinary artisan. Thus, each of the claimed features are taught or are at least suggested by the cited prior art.

### ***Response to Arguments***

Applicant's arguments filed March 24, 2008, and April 18, 2008, have been fully considered but they are not persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Specifically, Mitzutani is applied as secondary art to show that the techniques used by Applicants' claimed process are well known to those of skill in the art and not because they teach the precise process steps that are described in Applicants' claims. Hanson is applied to show the type of medium the microorganism cell line grows upon for and that it is obvious to select for well known culturing technique and media. It is the primary reference which reads on producing thrombinase.

Further, the argument that the pH range and culture medium provides for the production of thrombinase having a mw range of 31000 to 32000 daltons is noted, however, these conditions can be repeated in the art and one of skill would have been expected to provide for a thrombinase having a different mw based upon the conditions said production would be taking place. It would have been an obvious modification of the cited prior art to adjust molecular weight (mw) cut-off sizes in order to optimize thrombinase production and the size of the enzyme. The claims remain prima facie obvious over the cited prior art.

All claims fail to be patentably distinguishable over the state of the art discussed above and cited of record. Therefore, the claims are properly rejected.

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DEBBIE K. WARE whose telephone number is (571)272-0924. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/DKW/  
Deborah K. Ware  
Examiner  
Art Unit 1651

/David M. Naff/  
Primary Examiner, Art Unit 1657

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